

oxygen species and lipid peroxidation in the testis with concomitant decrease in sperm count and motility in a dose dependent manner. Activities of antioxidant enzymes catalase, superoxide dismutase and levels of reduced glutathione were found to be decreased in a dose dependent manner. Also, the levels of oxidized glutathione were increased leading to a shift in redox ratio. The testicular histomorphology was also altered dose dependently. Germ cell kinetic study revealed significant loss of various germ cell populations with increasing dose of quercetin. Interestingly, there was a reduction in germinal epithelium thickness concomitant with an increase in seminiferous tubule lumen diameter. In conclusion, the deleterious effects of quercetin on germ cells could be attributed to its pro-oxidant ability which might affect the sertoli cell functions.

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Kinematics and Kinetics of the Ciliary Waveform in Human Tracheal Epithelial Cells

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Cilia function is critical to human health. We developed quantitative methods to describe waveform, propulsive force, and net work of cilia on multi-ciliated human tracheal epithelial cells (HTEC).

Lung tracheobronchial epithelial cells were isolated from healthy donor subjects for culture and differentiated using growth factor-enriched medium and air-liquid interface conditions to yield multi-ciliated cells. Detached cells in 20 μ L of culture medium at room temperature were sandwiched between a glass slide and coverslip and lateral views of beating cilia were acquired (Zeiss Axiophot, 100X, oil immersion, DIC) for 2s at 100 fps (320x240 pixels, 15.07 pixels/ μ m). Waveforms were analyzed in N=21 cilia from 3 subjects. In each video frame, 30 points evenly distributed from the base to the tip of the cilium were fitted to a 4th-order polynomial curve. The resulting parameter sets were Fourier-transformed and filtered temporally to obtain a space-time surface representing a typical beat. Local velocity vectors and curvature were computed by differentiation of this surface, and local fluid forces on the cilium were estimated using resistive force theory: $f_N = C_{NV}v_N$ and $f_T = C_{TV}v_T$ ($C_N \approx 1.5 \times 10^{-3}$ pN-s/ μ m; $C_T \approx 0.7 \times 10^{-3}$ pN-s/ μ m). Power was calculated from the product $f \cdot v$. Beat frequency, curvature, and shear amplitude were also computed.

Waveforms of active cilia were asymmetric with distinct power and recovery strokes. The average propulsive force and work for active HTEC cilia were: $F_{prop} = 3.73 \pm 4.42$ pN, $W = 1.63 \pm 1.84$ aJ. We also identified apparently passive cilia with nearly symmetric waveforms and little propulsive effectiveness ($F_{prop} = -0.02 \pm 1.52$ pN, $W = 0.33 \pm 0.24$ aJ). Active cilia were longer (6.48 ± 0.66 vs 5.09 ± 0.73 μ m) and beat more rapidly (3.54 ± 0.77 Hz vs 2.64 ± 1.16 Hz) than passive cilia. It is not clear whether passive cilia are immature or simply represent normal heterogeneity. These results provide baseline data for future studies of motility defects.

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Dynamics of the Primary Cilium in Shear Flow

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In this work the equilibrium shape and dynamics of a primary cilium under flow are investigated using both theoretical modeling and experiment. The cilium is modeled as an elastic beam that may undergo large deflection due to the hydrodynamic load. Equilibrium results show that the anchoring effects of the basal body on the cilium axoneme behave as a nonlinear rotational spring. Details of the rotational spring are elucidated by coupling the elastic beam with an elastic shell. We further study the dynamics of cilium under shear flow with the cilium base angle determined from the nonlinear rotational spring, and obtain good agreement in cilium bending and relaxing dynamics when comparing between modeling and experimental results. These results potentially shed light on the physics underlying the mechanosensitive ion channel transport through the ciliary membrane.

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Optimizing the Energetic Efficiency of Ciliated Microorganisms

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Energetic efficiency of swimming has long been considered a non-issue in microorganisms, but newer studies show that ciliates can use more than half of their energy for propulsion. To estimate how close the ciliates are to the theoretically optimal way of swimming we address the following problems: i) we determine the optimal stroke of a cilium, ii) we determine the optimal

beating pattern of a ciliated surface and iii) we calculate the optimal shape of a ciliated swimmer.

For a single cilium we define the efficiency in a scale-invariant way and show that the optimal stroke consists of a working stroke with a stretched cilium and a recovery stroke where the cilium bends and moves closer to the surface. When optimizing an array of cilia we additionally show that metachronal waves improve the efficiency and that the optimal efficiency is achieved for antiplectic waves. The resulting beating patterns, as well as the optimal ciliary density, show remarkable similarity with those observed in ciliated microorganisms. In order to optimize the shape of the whole swimmer we use a simplified description where we replace the ciliated layer with a surface slip velocity. Depending on the curvature we allow, the optimal swimmer has an elongated shape, possibly with two protrusions along the symmetry axis. These optimal shapes again resemble those of different ciliates.

If we combine the results of our optimization with experimental efficiency estimates we can show that Paramecium has a propulsion efficiency that is within a factor of 2 of the theoretical optimum. This result suggests that ciliates have evolved for efficient swimming at different scales.

[1] N. Osterman and A. Vilfan, Proc. Natl. Acad. Sci. USA 108, 15727-15732 (2011)

[2] A. Vilfan, Phys. Rev. Lett. 109, 128105 (2012)

Cardiac Muscle I

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Alterations in Proteins Involved in Cellular Level Contractile Dysfunction in the Left Ventricles of Patients with End Stage Heart Failure

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Understanding how cellular level mechanical properties change as failing hearts remodel may help identify the protein modifications that produce contractile dysfunction associated with this condition. We therefore procured through wall left ventricular samples from patients undergoing heart transplants at the University of Kentucky and from organ donors who did not have heart failure. Multicellular chemically permeabilized preparations were subsequently obtained from sub epicardial, midwall and sub endocardial regions of these samples by mechanical homogenization and triton treatment. The mechanical properties of the preparations were assessed by attaching them between a force transducer and a motor and subjecting them to a standard series of mechanical assays. There was a 30% decrease in maximum power output (p-value = 0.01) and steady-state force (p-value=0.005) in patients with end-stage heart failure (n=8, total of 72 preparations) as compared to samples from nonfailing organ donors (n=4, total of 36 preparations). The phosphorylation of two cardiac sarcomeric proteins- myosin binding protein-C (cMyBP-C) and troponin-I (cTnI) which have been previously associated with contractile dysfunction were investigated using phospho specific antibodies. Western blot analysis of three major phosphorylated sites of cMyBP-C, P_{Ser273}, P_{Ser282} and P_{Ser302} were not significantly different between heart failure and non failing groups but cTnI phosphorylation at P_{Ser22/23} decreased significantly in heart failure (p=0.01). This study suggests that the cellular level mechanical dysfunction seen in heart failure may be in part due to phosphorylation modifications.

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Myocyte Power Output in Humans with End-Stage Heart Failure: Effects of LVAD Treatment

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